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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,757	02/11/2004	Michel Pairet	01-1174-1-C1	3466

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EXAMINER	
BADIO, BARBARA P	
ART UNIT	**PAPER NUMBER**
1628	

NOTIFICATION DATE	DELIVERY MODE
05/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

Office Action Summary	Application No.	Applicant(s)	
	10/776,757	PAIRET ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3,4,9,10,15-17,19-21,23,25,26,31-37,39 and 63-66 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3,4,9,10,15-17,19-21,23,25,26,31-37,39 and 63-66 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action on the Merits of a RCE

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Application

2. Claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 are pending in the present application and are rejected as indicated below.

Claim Rejections - 35 USC § 103

3. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

Applicant's argument is based on the showing of synergism of the combination of tiotropium and ciclesonide as claimed. According to applicant, (a) the prior art does not provide an expectation of said effect and (b) it is not necessary for applicant to provide a comparison to oxitropium/beclomethasone combination shown by Nishimura (reference was made to MPEP sec 716.02(a)(I)). Applicant's argument was considered but not persuasive for the following reasons.

The examiner agrees that a showing of synergism can overcome a prima facie case of obviousness. However, contrary to applicant's position that it is necessary for

applicant to provide a comparison to the prior art composition, MPEP § 716.02(a)(I) further states:

> a greater than additive effect is not necessarily sufficient to overcome a *prima facie* case of obviousness because such an effect can either be expected or unexpected. Applicants must further show that the results were greater than those which would have been expected from the prior art to an unobvious extent, and that the results are of a significant, practical advantage. *Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991)

Applicant has not shown that the results are "greater than those which would have been expected from the prior art to an unobvious extent and that the result are of a significant, practical advantage".

As noted in the previous Office Actions, Nishimura provides a motivation to use the combination of an anticholinergic agent and a corticosteroid by the teaching of beneficial effect of said combination. Applicant argues said effect is minor and there is no allegation or proof that the advantages are more than merely additive effect. However, the issue is not whether the effect is minor but whether based on the teachings of the cited prior art, the combination of tiotropium (an anticholinergic agent) and ciclesonide (a steroid) would have been obvious to the skilled artisan in the art at the time of the present invention. The examiner position is that said is obvious based on the combined teachings of the cited references as discussed in the previous Office Actions. Applicant's showing of unexpected result is not persuasive because it does not show the results are greater than those expected from the prior art as required by MPEP § 716.02. MPEP § 716.02(e) clearly states:

> An affidavit or declaration under 37 CFR 1.132 must compare the claimed subject matter with the closest prior art to be effective to rebut a *prima facie* case of obviousness. *In re Burckel*, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979). "A comparison of the *claimed* invention with the disclosure of each cited reference to determine the number of claim limitations in common with each reference, bearing in mind the relative importance of particular limitations, will usually yield the closest single prior art reference." *In re Merchant*, 575 F.2d 865, 868, 197 USPQ 785, 787 (CCPA 1978) (emphasis in original). Where the comparison is not identical with the reference disclosure, deviations therefrom should be explained, *In re Finley*, 174 F.2d 130, 81 USPQ 383 (CCPA 1949), and if not explained should be noted and evaluated, and if significant, explanation should be required. *In re Armstrong*, 280 F.2d 132, 126 USPQ 281 (CCPA 1960) (deviations from example were inconsequential).

Lastly, one can not make comparison of results obtained in humans (Nishimura) with that obtained in laboratory animals (beagle dogs). Thus, a comparison of the prior art composition in beagle dogs under identical conditions as that presented for the claimed composition is required to evaluate applicant's argument of unexpected results based on synergism.

In summary, Nishimura teaches an advantage to the utilization of a combination of an anticholinergic agent and a corticosteroid in the treatment of asthma, Banholzer teaches tiotropium and salts thereof as strong anticholinergic agents for use in treating asthma and, thus, the use of tiotropium and a known corticosteroid such as ciclesonide would have been prima facie obvious to the skilled artisan in the art at the time of the present invention. The motivation is based on the teaching of Nishimura of advantageous effect of the combination versus corticosteroid alone. Applicant's argument of unexpected results is not persuasive because it lacks comparison with the

prior art composition and, thus, a showing that the results obtained by the claimed combination is greater than would have been expected from the prior art.

For these reasons and those given in the previous Office Actions, the rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

4. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 103 over Keller et al. (WO 00/28979, see English equivalent US 6,645,466), Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

Applicant's argument against Nishimura and Banholzer are as discussed above in #3.

Applicant argues Keller fails to provide any teaching which makes up for the deficiencies of Nishimura and Banholzer. According to applicant, Keller provides no suggestion to combine tiotropium, ciclesonide and one of the specific excipients recited by the claimed invention and further provides no hint that such a combination would provide unexpected synergistically advantageous properties as shown by applicants. Applicant's argument was considered but not persuasive for the following reasons.

As noted above in #3, Nishimura teaches an advantage to the utilization of a combination of an anticholinergic agent and a corticosteroid in the treatment of asthma, Banholzer teaches tiotropium and salts thereof as strong anticholinergic agents for use

in treating asthma and, thus, the use of tiotropium and a known corticosteroid such as ciclesonide would have been prima facie obvious to the skilled artisan in the art at the time of the present invention.

Keller, as discussed in the previous Office Actions, was utilized in combination with Nishimura and Banholzer for its teaching of an inhalable powder formulation comprising an anticholinergic agent such as tiotropium and a corticosteroid such as ciclesonide as well as the use of excipients as recited by the instant claims. Based on the teaching of Nishimura and Banholzer, the utilization of the formulation of Keller for treatment of asthma would have been obvious to the skilled artisan in the art at the time of the present invention. Keller provides the suggestion to combine tiotropium, ciclesonide and the excipients recited by the claimed invention by teaching each in the production of dry powder formulations.

As to applicant's argument that the reference does not provide any hint that such a combination would provide unexpected synergistically advantageous properties, applicant attention is directed to Nishimura. Nishimura as discussed previously, teaches the combination of an anticholinergic with a corticosteroid is advantageous in the treatment of asthma and, thus, provide the motivation to utilize the formulation of Keller in the treatment of asthma.

Lastly, applicant has not provided evidence of unexpected results in comparison with the combination as taught by the prior art. Absence said showing, the claimed invention is prima facie obvious.

For these reasons and those given in the previous Office Actions, the rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 103 over Keller et al. (WO 00/28979, see English equivalent US 6,645,466), Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/
Primary Examiner, Art Unit 1628